Remarks/Arguments

Applicants respectfully traverse and request the consideration of all rejections in the office action mailed on November 28, 2005.

I.   *Rejection – 35 U.S.C. section 103(a)*

The Examiner has rejected claims 10, 11, 13, and 14 under 35 U.S.C. section 103(a) as obvious over Hammond in view of Tizard. The Examiner acknowledges that Hammond does not disclose: (1) the element in claims 10 and 13 of obtaining first and second images and subtracting the images (i.e. B-A) on a pixel-by-pixel basis to create a third image; and (2) the element in claims 11 and 14 of applying the formula (B-A)/A to obtain the third image. The Examiner states that Tizard discloses the use of B-A on a pixel-by-pixel basis, and further, that Tizard refers to adjusting for overexposure which would read on the /A step. (Office Action, page 6.)

A.   *Tizard Does Not Disclose the Formula (B-A)/A.*

As to the Examiner's first point, that Tizard discloses B-A on a pixel-by-pixel basis, Tizard does disclose subtraction of one image from the other image (i.e., B-A). Applicants do not believe that Tizard specifically states that a pixel-by-pixel subtraction is performed; however, Applicants do not contest this point in light of the amendments that are made in this response.

As to the second point, that Tizard discloses the /A step, Applicants respectfully disagree. Applicants have amended claims 10 and 13 to include the limitation, from claims 11 and 14, respectively, of applying the formula (B-A)/A to create the third image,

and have cancelled claims 11 and 14. Claims 10 and 13 are patentable over Hammond in view of Tizard because Tizard does not disclose the /A step.

Tizard does not mention dividing the subtracted image (B-A) by A. Tizard states that: "the DiffScreen program subtracts the grey values for the first image from the grey values of the second image, and the absolute values are used to generate a new picture...that shows the differences between the two autoradiographs. Imaging artifacts arising from misalignment of the autoradiographs and autoradiographs with significantly different exposure times are avoidable." (Tizard, page 209.) Tizard says nothing about dividing the subtracted result (the third image) by A (i.e., applying the formula (B-A)/A to create the third image, image C.)

As set forth in the accompanying Declaration of Alan L. Lehman, Tizard's mention of "avoiding different exposure times" does not disclose the formula (B-A)/A. Overexposure compensation only requires a single image whereas Applicants' method requires two images to produce the desired result. Moreover, exposure compensation is a linear transformation – the value of each individual pixel is reduced by a fixed amount to obtain the desired exposure. (B-A)/A is a non-linear transformation; the magnitude of change is highly dependant on the starting values. (Lehman Declaration, paragraph 3.)

Thus, claims 10 and 13 are not obvious based on Hammond in view of Tizard. The rejection under section 103(a) should be withdrawn.

B. Unexpected Results

Declarations with evidence of unexpected results and other factors must be considered by the Examiner to determine obviousness under section 103 (M.P.E.P.

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section 716.01(a).) The declaration of Dr. Lehman contains factual evidence that is

highly relevant and demonstrates the nonobviousness of Applicants' invention.

As set forth in Dr. Lehman's declaration, the formula (B-A)/A yields significant

advantages over the simple subtraction formula B-A, which is disclosed by Tizard. The

formula B-A does not distinguish between data pairs consisting of A pixel values that start low

and B pixel values that end high, and A values that start high and B values that end higher. For

example, using the B-A formula, it is impossible to distinguish the mathematical results for the

following pairs of A and B pixel values: A=1 and B=51 versus A=25 and B=75. The

mathematical result obtained from B-A for both pairs of pixel values is 50. In contrast to the

results obtained from B-A; the (B-A)/A formula produces dramatically different mathematical

results. For A=1 and B=51, the result is 50; while for A=25 and B=75, the result is 2. Thus,

there is a significant difference in the mathematical results that depends on whether the A pixel

value is high or nearly zero. The formula (B-A)/A clearly distinguishes between those same data

pairs by diminishing the mathematical result of any A and B pixel value pairs where the A value

is not low. (Lehman Declaration, paragraph 4.)

As further discussed by Dr. Lehman, this distinction is critical in the use of this

method in determining the differences between the molecular interactions of two

different mixtures of molecules, for example, a first mixture of protein extract from

normal cells and a target mixture of protein extract from cancer cells. Image A shows

beads that bound molecules of the first mixture (which could include molecules unique to

the first mixture and molecules common to both the first mixture and the target mixture)

and beads that are false positives (beads that bound reagents used in the method). Image

B shows all of the beads of image A plus beads that bound molecules unique to the target

mixture. Image C is created by applying the formula (B-A)/A on a pixel-by-pixel basis, and it shows those beads that bound molecules unique to the target mixture (true positives). The /A step emphasizes the true positive beads by giving much greater weight to beads not marked in image A but marked in image B, and lesser weight to beads marked in both image A and image B. In other words, greater weight is given to beads that have bound molecules unique to the target mixture than beads that have bound molecules common to both mixtures. Where, for example, the first mixture is a normal cell extract and the target mixture is a cancer cell extract, this distinction is of crucial significance because it identifies the beads (and therefore the ligands) that bind molecules that are unique to cancer cells. (Lehman Declaration, paragraph 4.)

II. *Conclusion*

In view of the above, Applicants respectfully request that the Examiner pass this case to issue.

Dated: November 15, 2006   Respectfully submitted,

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